

DNA and CHROMOSOMES

DNA Structure and Replication

Experiments

- Miescher
 - First to isolate and identify nucleic acids
- Garrod
 - First to link inheritance in humans and proteins
- Griffith
 - Took first step in identifying DNA as the genetic material by discovering transformation
- Avery, MacLeod, McCarty
 - Determined DNA is the substance that caused the bacterial transformation in Griffith's experiment

Discovery of Bacterial Transformation

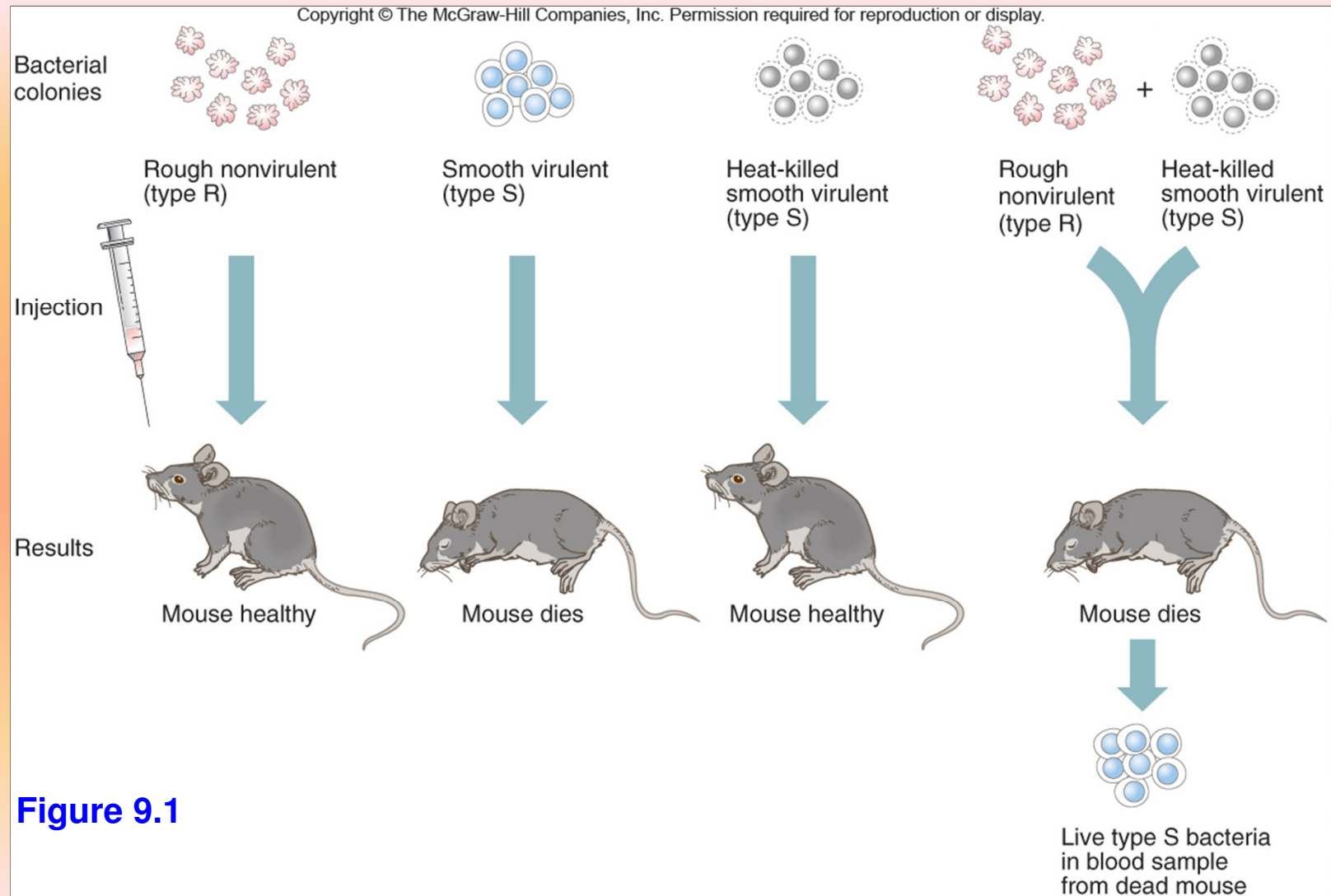


Figure 9.1

The Transforming Principle

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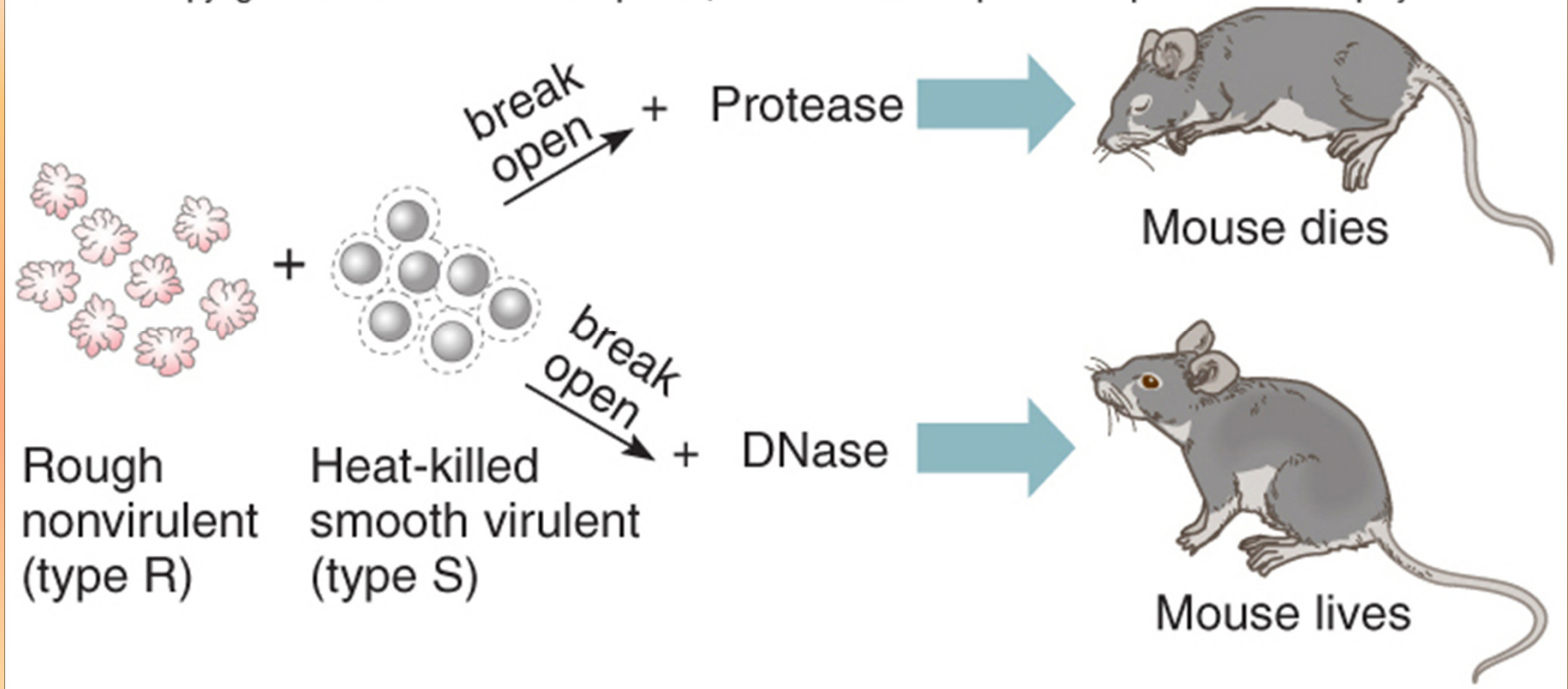
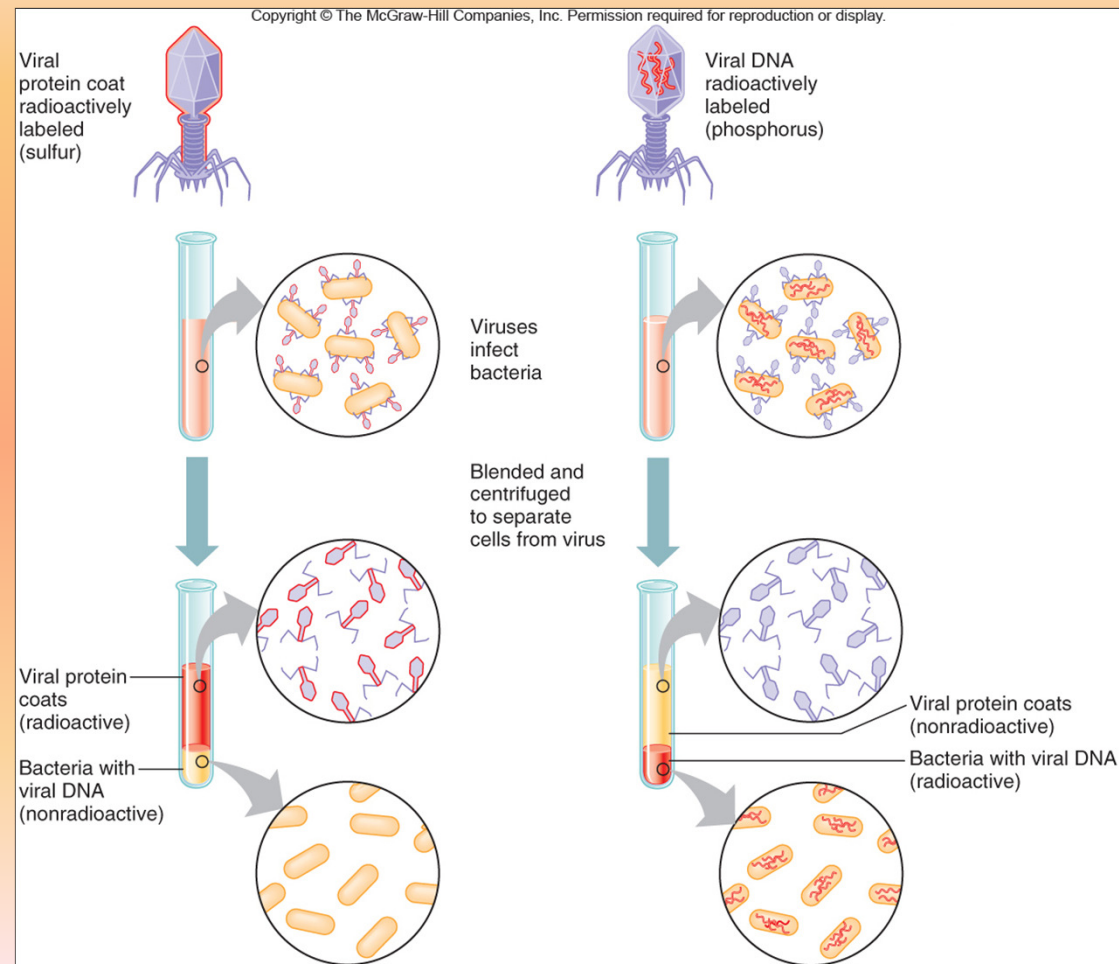


Figure 9.1

Figure 9.2

- Hershey and Chase
 - Confirmed DNA is the genetic material using radioactive isotopes in viruses

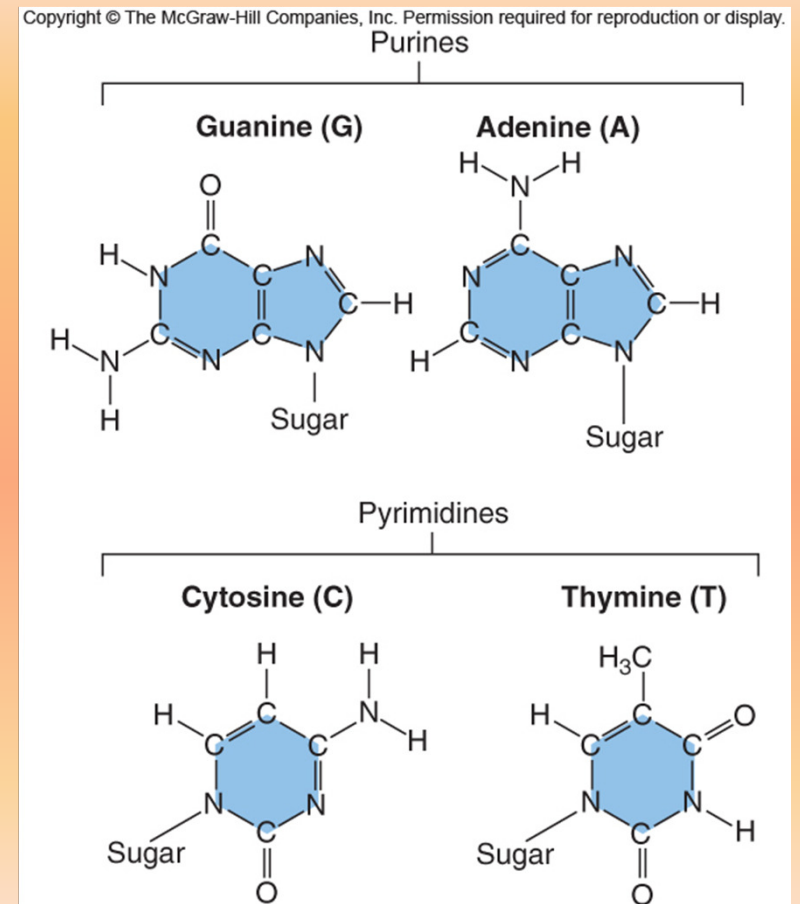
Figure 9.3



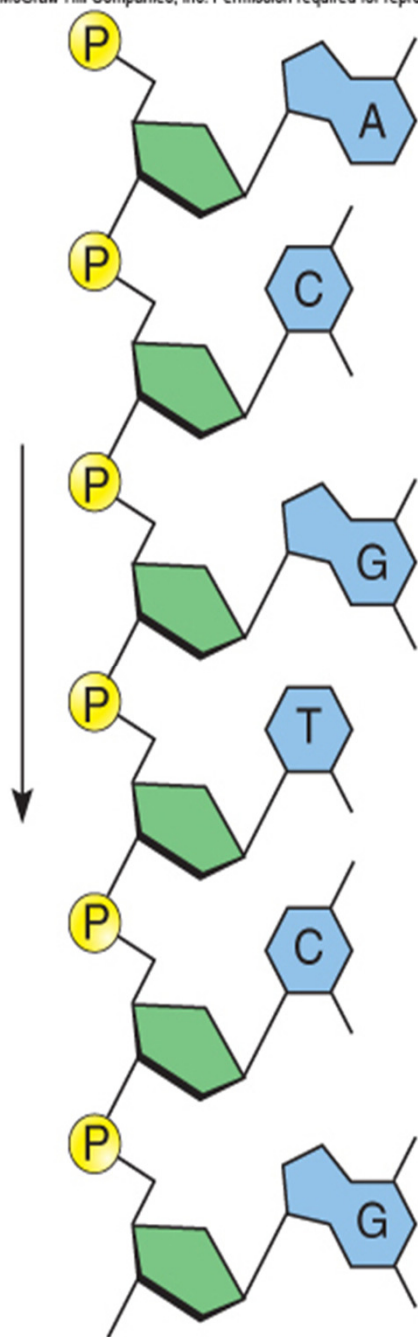
- Levene
 - Identified deoxyribose as the sugar in DNA
 - Realized sugar-phosphate proportions were always the same and there are 4 types of nitrogen-containing bases
- Chargraff
 - Determined that a given sample of DNA contains equal amounts of adenine and thymine as well as equal amounts of guanine and cytosine
- Wilkins and Franklin
 - Work with X ray diffraction contributed to determination of DNA double helix
- Watson and Crick
 - Determined 3-D structure of DNA double helix

DNA Structure

- Building blocks = nucelotides
 - 1 deoxyribose sugar
 - 1 phosphate group
 - 1 nitrogenous base
 - Purines (2 ring structure)
 - Adenine (A)
 - Guanine (G)
 - Pyrimidines (single ring)
 - Cytosine (C)
 - Thymine (T)

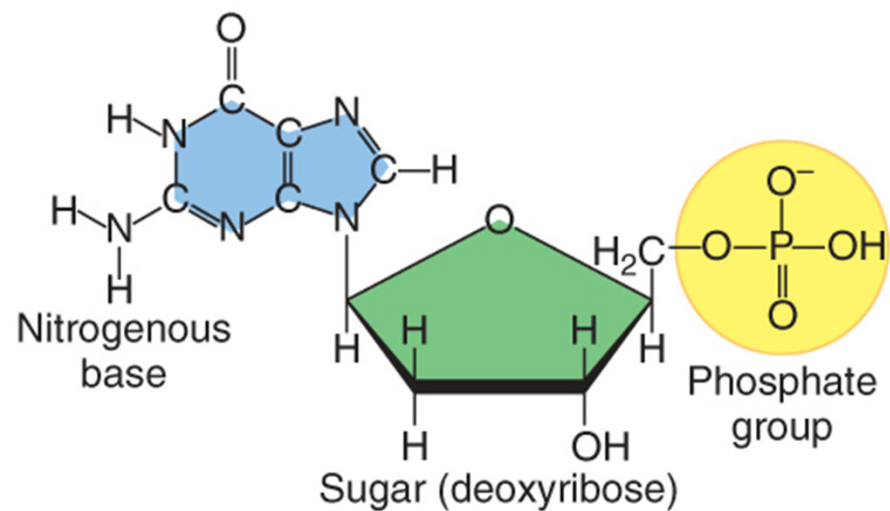


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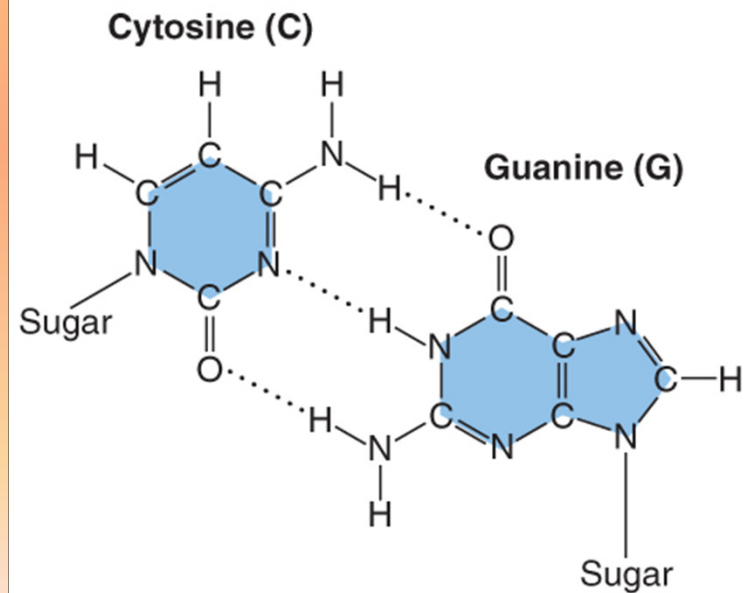
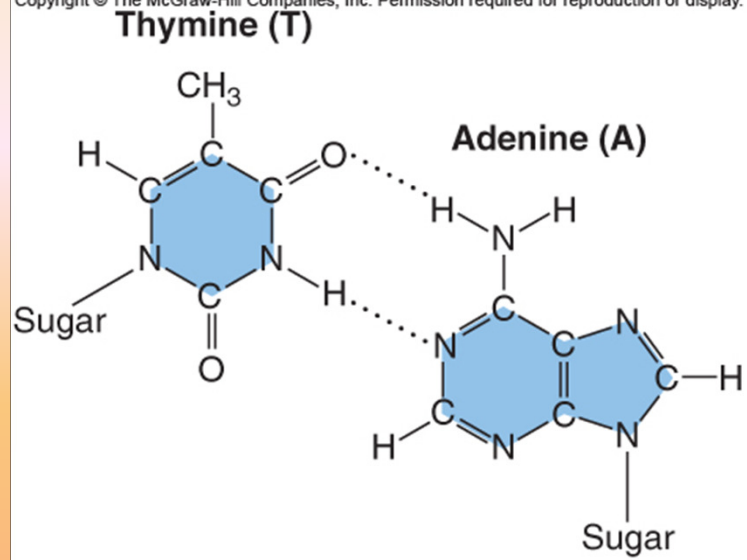
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Guanine (G)

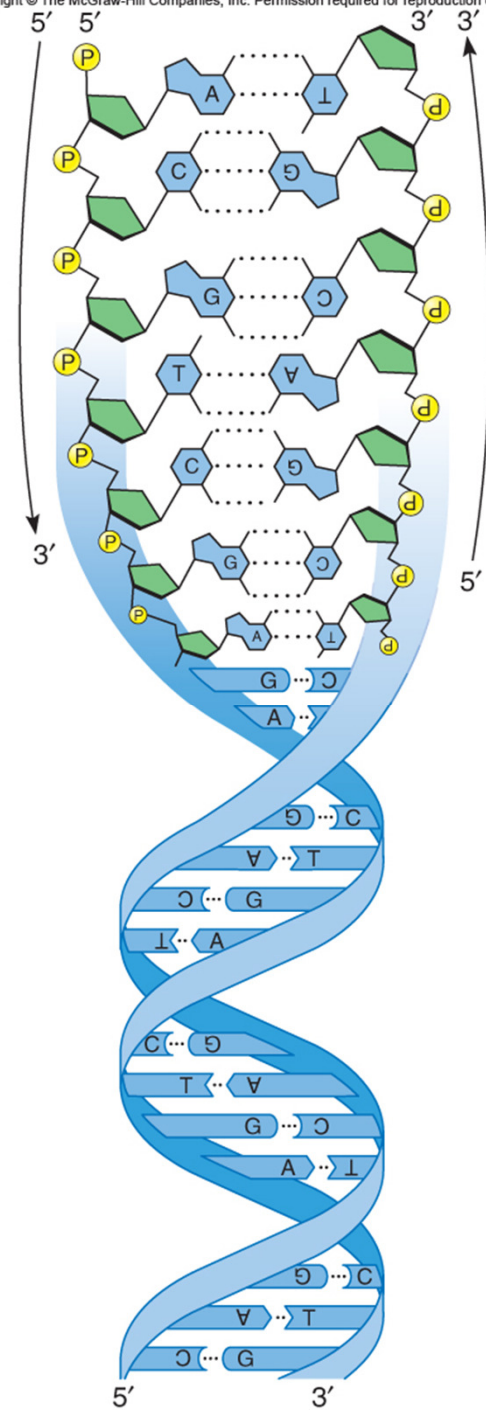


- Nucleotides join to form long chains
 - Sugar-phosphate backbone
 - Strands are antiparallel
 - 5 prime (5') and 3 prime (3') ends
 - Nitrogenous bases held to those of 2nd strand by hydrogen bonds
 - Complementary base pairs
 - A bonds with T
 - C bonds with G
- Double helix forms when antiparallel, base-paired strands twist

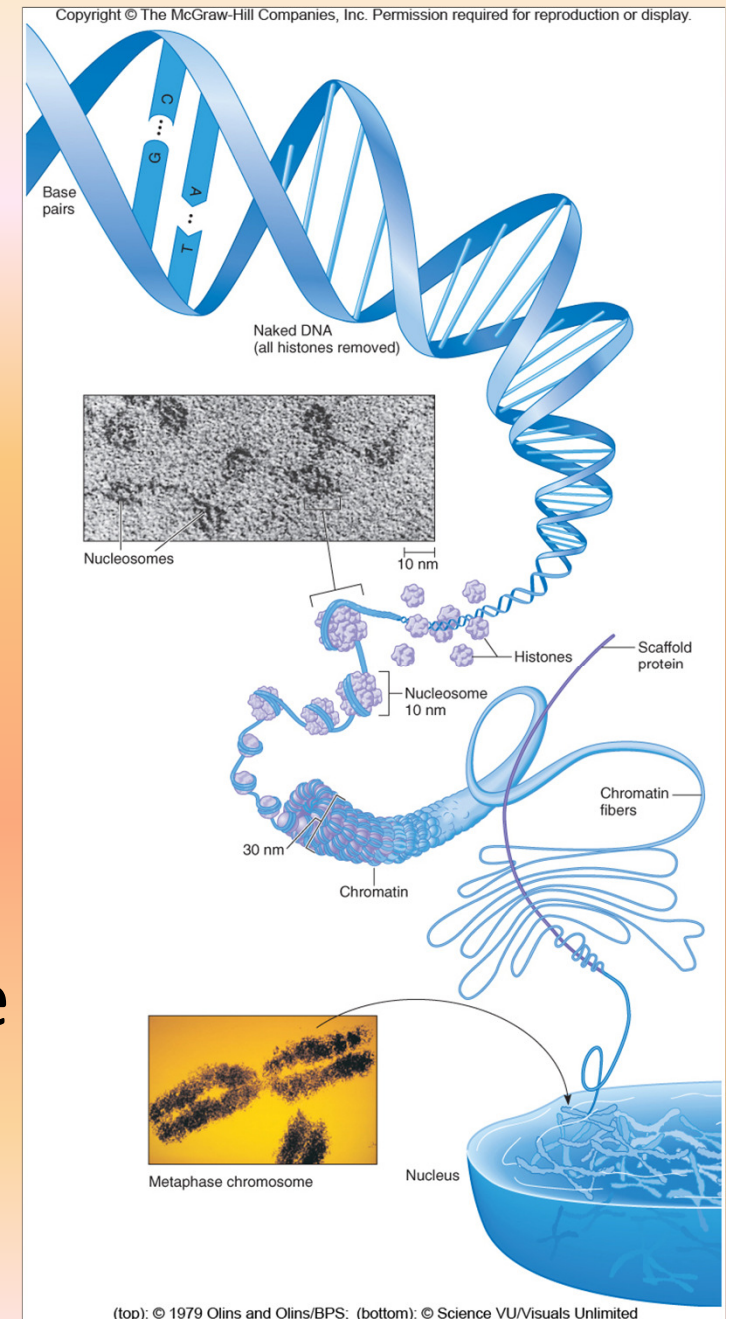
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- DNA coils around proteins called **histones**
 - “Beads-on-a-string”-like structure
 - **Nucleosome** =
 - Unit of chromatin structure
 - “Bead” part
- DNA wraps at several levels, compacting into a chromosome
 - Very tightly packed during mitosis



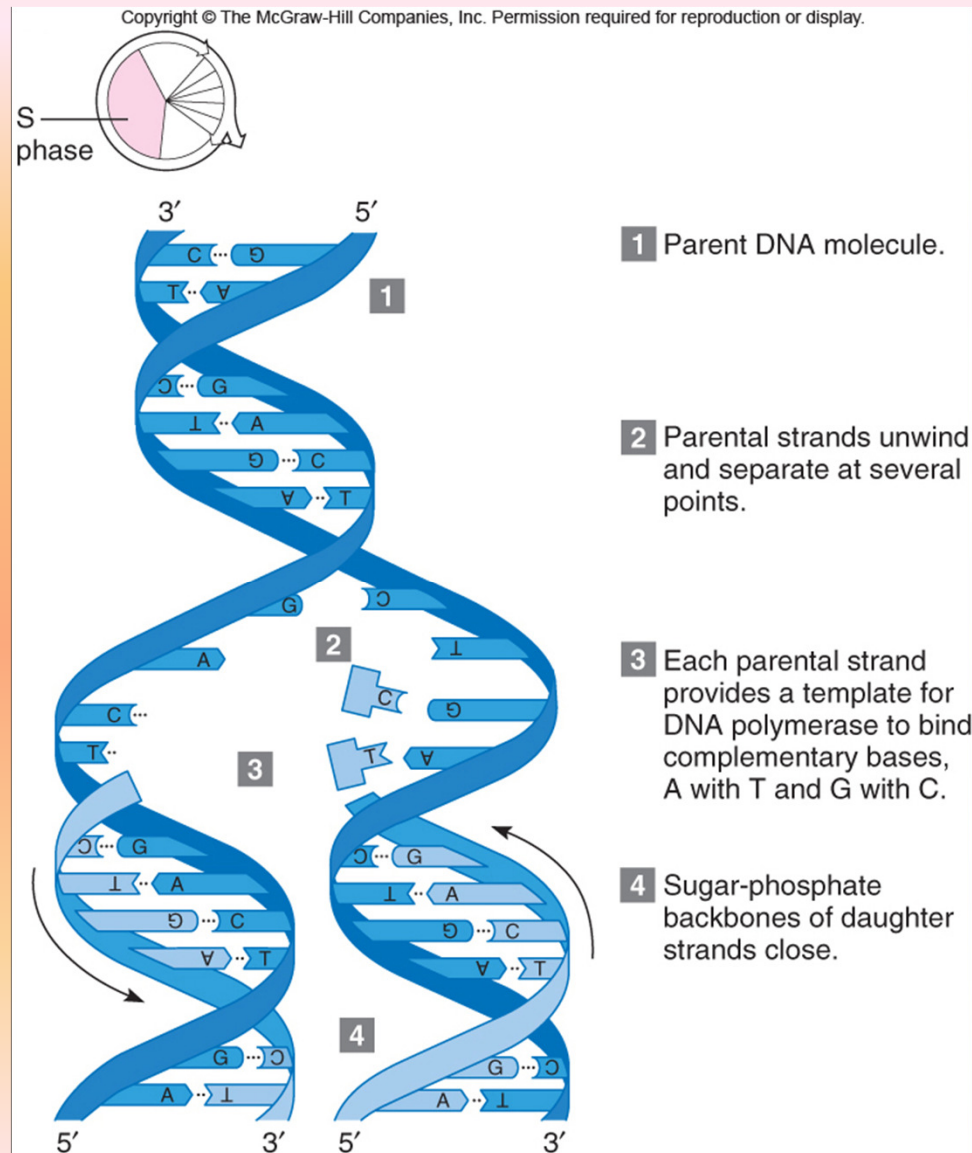
- Altogether, the chromosome substance is called **chromatin**=
 - 30% histone proteins
 - 30% DNA scaffold and other proteins that bind DNA
 - 30% DNA
 - 10% RNA

DNA Replication

- **Semiconservative replication** =
 - DNA synthesis along each half of the double helix
 - New DNA double helix conserves half of the original
- Overview
 - Parental strands unwind and separate at several points
 - Each parental strand provides a template for DNA polymerase to bind complementary bases
 - A with T and vice versa
 - G with C and vice versa
 - Sugar-phosphate backbones of daughter strands close

Overview of DNA Replication

Figure 9.15



- DNA replication occurs simultaneously at several points on each chromosome, and the pieces join
- **Initiation site** =
 - Site where DNA replication begins on a chromosome
- **Replication fork** =
 - Locally opened portions of a replicating DNA double helix



- Activities at the replication fork
 1. **Helicase** unwinds and separates strands
 - Binding proteins stabilize and keep strands apart
 2. **Primase** makes a short stretch of RNA on the DNA template
 - **RNA primer** is a short sequence of RNA that initiates DNA replication
 3. **DNA polymerase** adds DNA nucleotides to the RNA primer
 - Also proofreads and corrects mismatched base pairs
 4. **Exonuclease** removes RNA primers
 5. **Ligase** joins Okazaki fragments and seals sugar-phosphate backbone

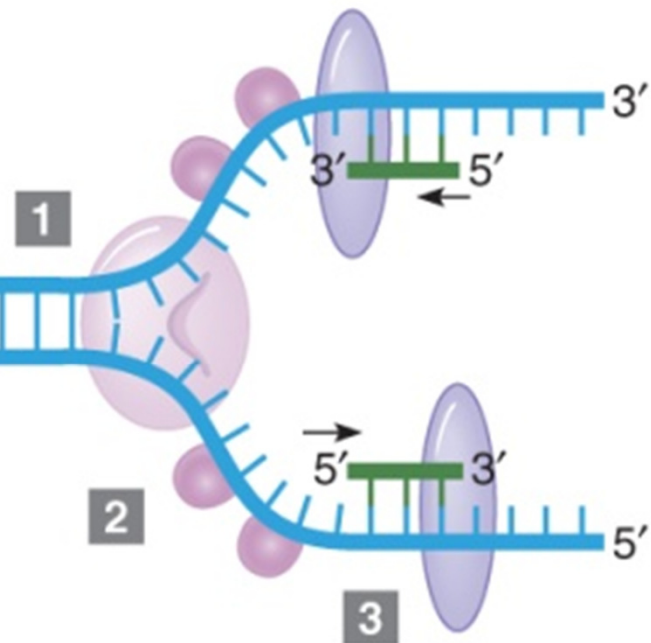
Activities at the Replication Fork

1 Helicase binds to origin and separates strands.

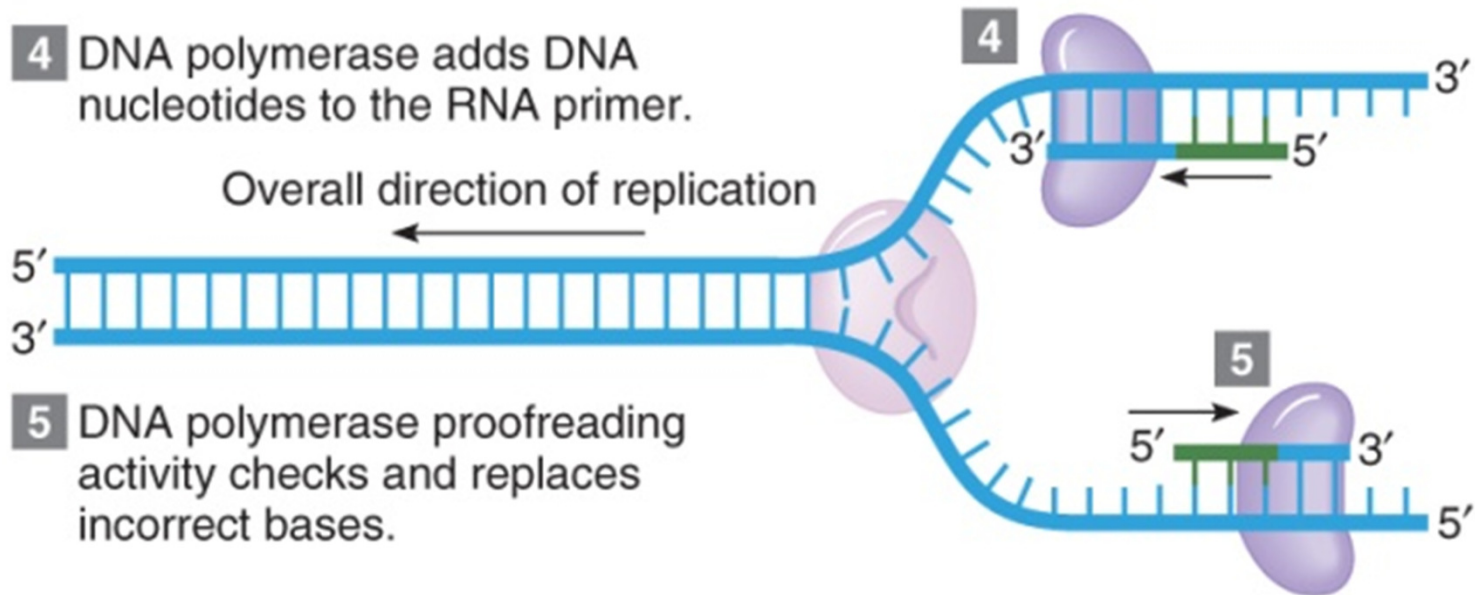
5'
3'

2 Binding proteins keep strands apart.

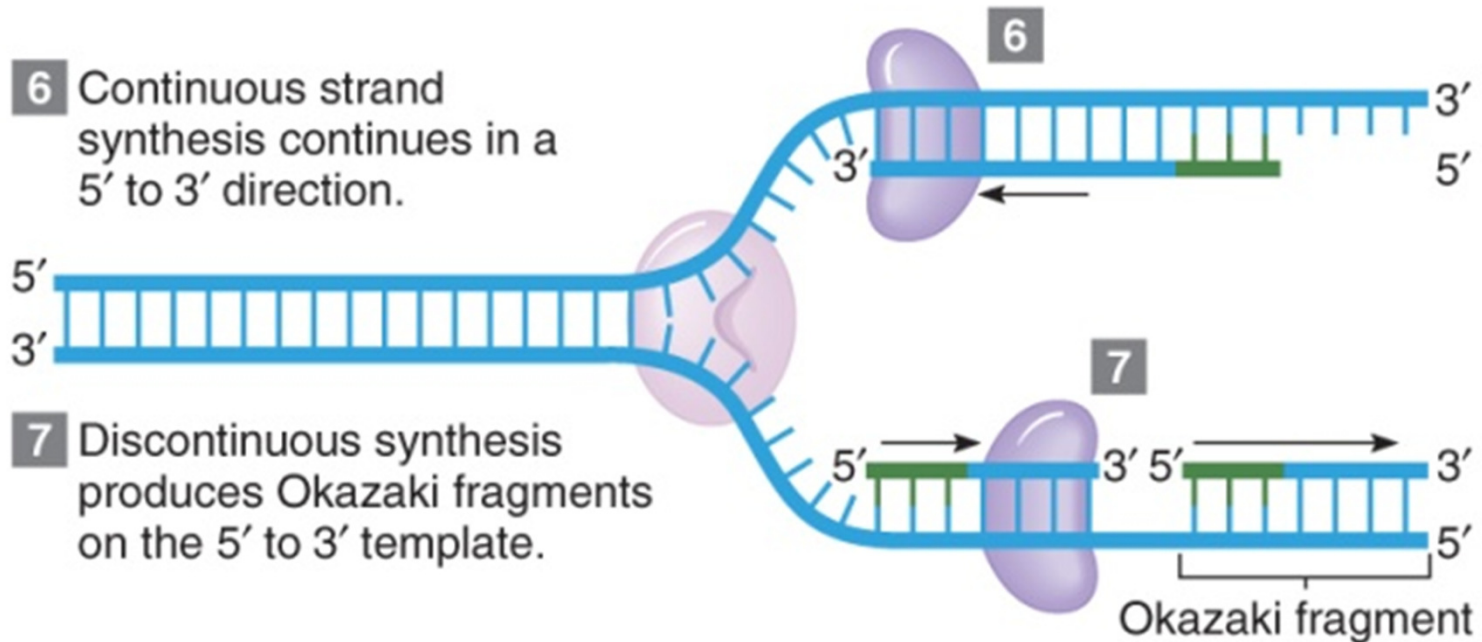
3 Primase makes a short stretch of RNA on the DNA template.



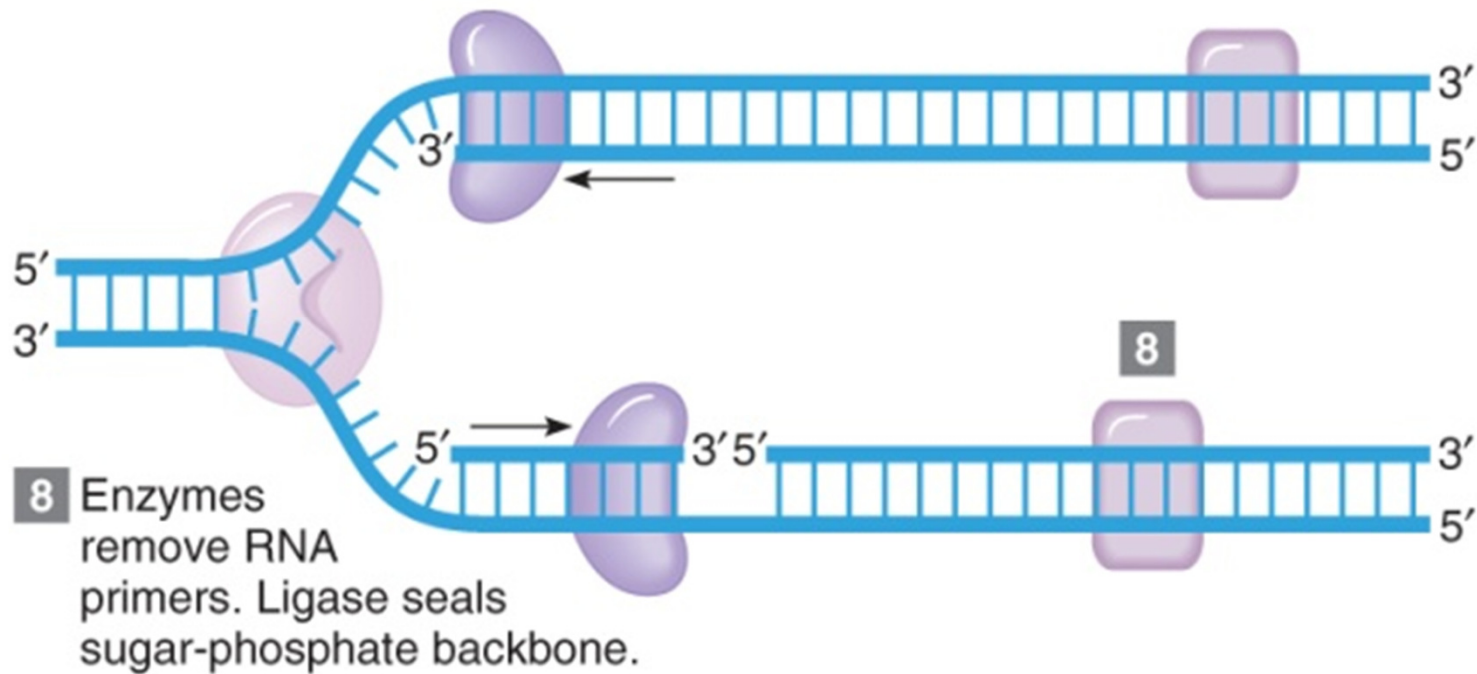
Activities at the Replication Fork



Activities at the Replication Fork



Activities at the Replication Fork



- DNAP works directionally
 - Only adds new nucleotides to exposed 3' end
 - Replication proceeds in a 5' to 3' direction
 - Replication on one strand is continuous
 - The other is discontinuous
 - Produces small pieces called **Okazaki fragments**

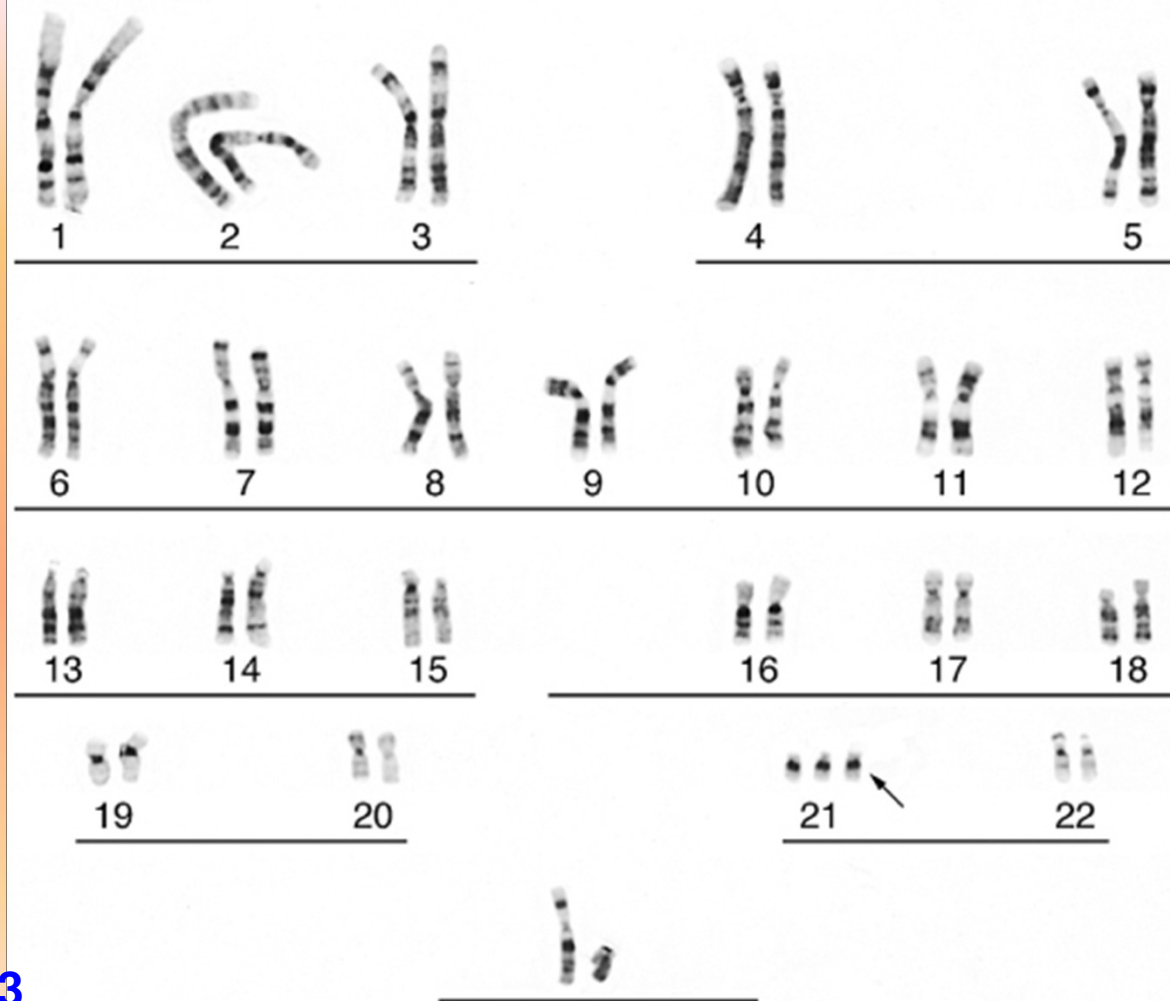
Chromosomes

Portrait of a Chromosome

- **Cytogenetics** =
 - Links chromosome variations to specific traits and illnesses
- **Karyotype** =
 - Chromosome chart
 - Displays chromosomes in pairs by
 - Size
 - Physical landmarks that appear during metaphase

Karyotype

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Sex chromosomes

Courtesy National Human Genome Research Institute

Figure 13.3

- Human chromosomes are numbered from largest to smallest (1-22)
 - Other 2 chromosomes are X and Y
- Centromere position distinguishes chromosomes as well

- **Metacentric** =

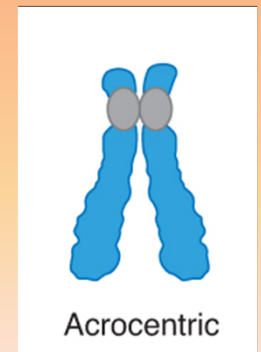
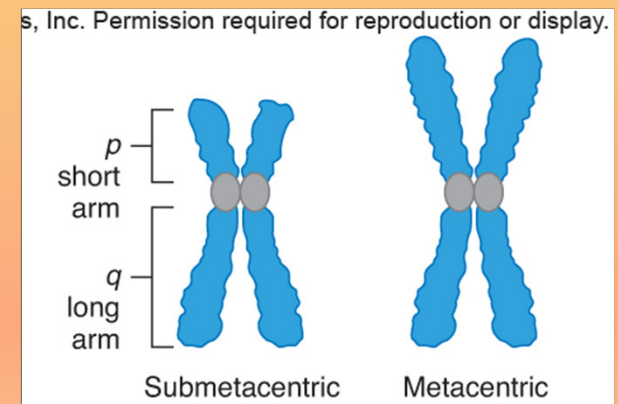
- 2 arms of approx. equal length

- **Submetacentric** =

- One long arm (***q***) and one short arm (***p***)

- **Acrocentric** =

- Pinches off only a small amount of material toward one end



Atypical Chromosome Number

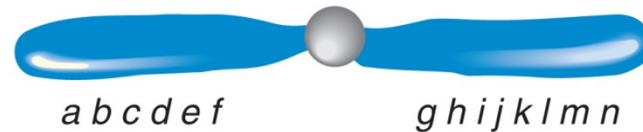
- **Polyploid** =
 - A cell with one or more extra sets of chromosomes
- **Aneuploid** =
 - A cell with one or more extra or missing chromosomes
 - **Monosomy** =
 - One chromosome absent
 - **Trisomy** =
 - One chromosome extra
- **Nondisjunction** =
 - Unequal partition of chromosomes into gametes during meiosis
 - Chromosome pair fails to separate during anaphase

- Autosomal Aneuploids
 - Trisomy 21
 - Down syndrome
 - Trisomy 18
 - Edward syndrome
 - Trisomy 13
 - Patau syndrome

- Sex Chromosome Aneuploids: Female
 - XO Syndrome
 - Turner syndrome: Lags in sexual development
 - Triplo-X
- Sex Chromosome Aneuploids: Male
 - XXY Syndrome
 - Klinefelter syndrome: Underdeveloped sexually
 - XXYY Syndrome
 - Extra set of both sex chromosomes
 - Infertile
 - XYY Syndrome
 - Jacobs syndrome
 - Note: Y with no X is nonviable

Atypical Chromosome Structure

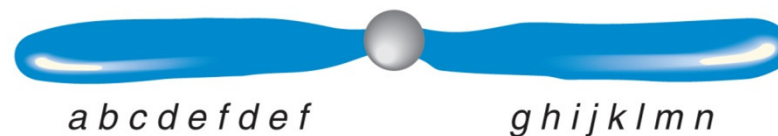
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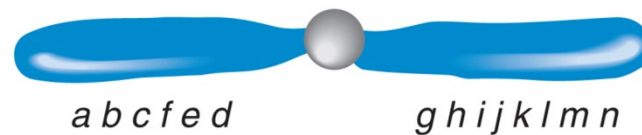
a. Normal sequence of genes



b. Deleted sequence of genes



c. Duplicated sequence of genes



d. Inverted sequence of genes

- **Deletion** =
 - Missing sequence of DNA
 - Example: Cri-du-chat syndrome (5p-)
- **Duplication** =
 - Extra copy of a DNA sequence
- **Translocation** =
 - Exchange between nonhomologous (different) chromosomes
 - **Translocation carrier** =
 - Individual with exchanged chromosomes but no signs or symptoms
 - Has the usual amount of genetic material, but it is rearranged



Courtesy, KathyNaylor

- 2 major types of translocations

- 1. Robertsonian translocation** =

- 2 short arms of nonhomologous chromosomes break and the long arms fuse, forming one unusual, large chromosome

- Example: Translocation Down Syndrome

- 2. Reciprocal translocation** =

- 2 nonhomologous (different) chromosomes exchange parts

- Rare type of translocation

- 1. Insertional translocation** =

- Part of one chromosome inserts into a nonhomologous chromosome

- **Inversion** =

- Inverted sequence of chromosome bands

- **Paracentric inversion** =

- Inverted chromosome that does not include the centromere

- **Pericentric inversion** =

- Inverted chromosome that includes the centromere

Segregation of a Paracentric Inversion

Figure 13.20

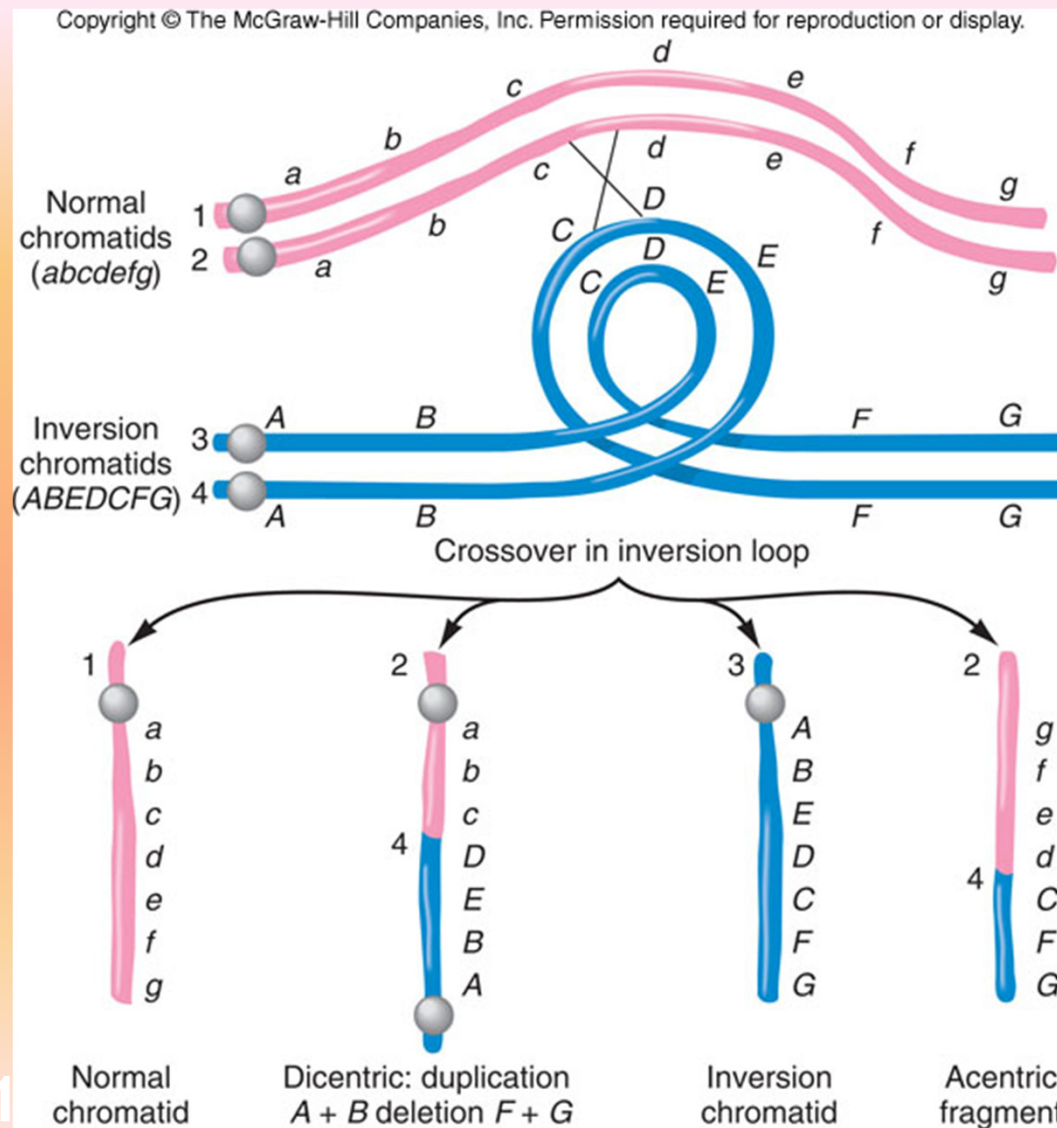


Figure 13.21

Segregation of a Pericentric Inversion

Figure 13.21

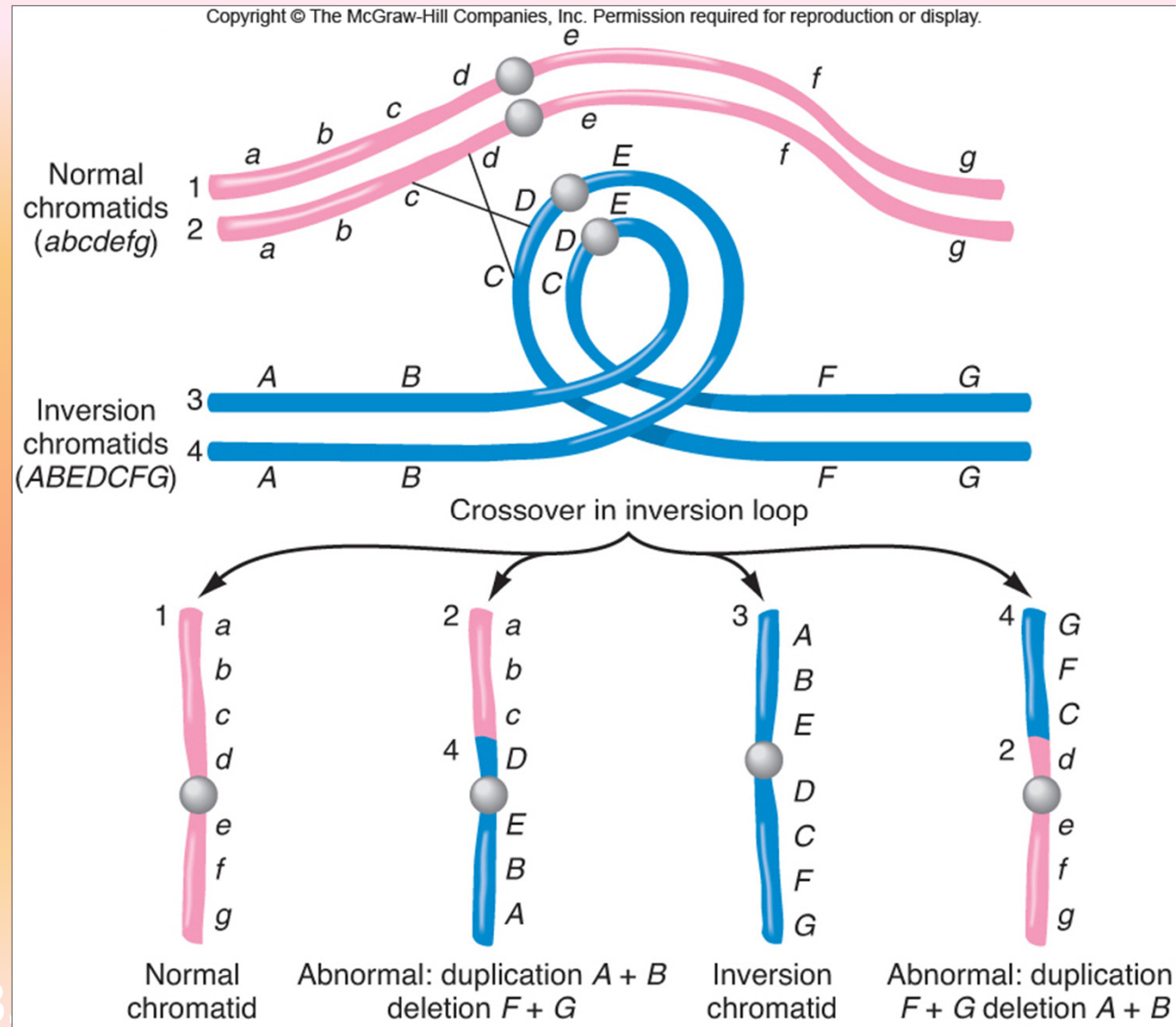


Figure 13

- **Isochromosome** =
 - Chromosome has identical arms
- **Ring Chromosome** =
 - Chromosome loses telomeres and the ends fuse, forming a circle
- **Uniparental disomy** =
 - Inheriting 2 copies of the same gene from one parent

